REMARKS

By the present Amendment, Applicants have canceled pending Claims 1-273 in favor of newly added Claims 274-277. Claims 1-273 are canceled without prejudice or disclaimer as to the subject matter contained therein. Applicants reserve the right to file continuation and/or divisional applications on all or a portion of the subject matter which was canceled by this Amendment.

Claims 274 and 276 are essentially copied from Claim 35 of U.S. Patent Nos. 6,358,709 ("the '709 patent") to Short *et al.* ("Short"), which incorporates the limitations of Claims 32 and 33 of the '709 patent. Claims 275 and 277 are essentially copied from Claim 18 of U.S. Patent No. 6,238,884 ("the '884 patent") to Short, which incorporates the limitations of Claim 1.

Specific support for each element of Claims 274-275 in the present application can be found in **Appendix A**, attached hereto. Support for Claims 276 and 277 is the same as that for Claims 274 and 275, respectively. A copy of U.S. Patent No. 6,177,679, which issued from U.S. Application Serial No. 08/621,859 (incorporated by reference in its entirety for all purposes at page 1, ll. 12-19) is submitted herewith for the Examiner's convenience.

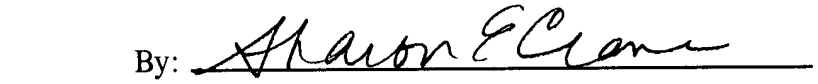
Because Claims 274 and 276 are to the same or substantially the same subject matter as Claim 35 of the '709 patent, and because Claims 275 and 277 are to the same or substantially the same subject matter as Claim 18 of the '884 patent, and such claims are being made within

one year from the date on which the '709 and '884 patents were granted (*i.e.*, March 19, 2002 and May 29, 2001, respectively), 35 U.S.C. § 135(b) is satisfied.

Based on the present amendments to the claims, Applicants intend to file a Request for Interference Pursuant to 37 C.F.R. §1.607, in which all of the claims of the '709 and '884 patents correspond to the Count. However, in order to simplify matters prior to that submission, Applicants respectfully request that after an initial review of the present Amendment, but prior to examination on the merits, the Examiner contact the undersigned regarding scheduling of a personal interview on the present application.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: 

R. Danny Huntington
Registration No. 27,903
Sharon E. Crane, Ph.D.
Registration No. 36,113
Mercedes K. Meyer, Ph.D.
Registration No. 44,939

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620

Date: May 29, 2002

APPENDIX A

New Claim Chart

New Claims 274-275	Support in the Specification[1]
274. A method for producing a mutant molecule having at least one desired property, the method comprising:	One aspect of the invention is a method for evolving a protein encoded by a DNA substrate molecule comprising... screening or selecting the products of (b) for a desired property... (Page 2, ll. 12-21)

New Claims 274-275	Support in the Specification[1]
(a) subjecting a plurality of parental polynucleotides to simultaneous mutagenesis so as to produce a plurality of mutant polynucleotides, wherein the mutagenesis comprises subjecting a codon-containing template polynucleotide to amplification using	In some embodiments of the invention, sequence information from one or more substrate sequences is added to a given "parental" sequence of interest, with subsequent recombination between rounds of screening or selection. Typically, this is done with site-directed mutagenesis performed by techniques well known in the art... (Page 39, ll. 23-28) The "cassette" can be generated several different ways: A) by annealing two oligonucleotides together and converting them into double stranded DNA; B) by first amplifying segments of DNA with oligonucleotides that carry randomized sequences and then reamplifying the DNA to create the cassette for cloning; C) by first amplifying each half of the DNA segment with oligonucleotides that carry randomized sequences, and then heating the two pieces together to create the cassette for cloning; and D) by error-prone PCR. The cassettes formed by these four procedures are fixed in length and coding frame, but have codons which are unspecified at a low frequency. Thus, cloning and expression of the cassettes will generate a plurality of peptides or proteins that have one or more mutant residues along the entire length of the cassette. (Col. 85, l. 60 - Col. 86, l. 10 of U.S. Patent No. 6,117,679 ("the '679 patent"), which issued from Serial No. 08/621,859, incorporated by reference in its entirety for all purposes at p. 1, l. 12 of the specification)

New Claims 274-275	Support in the Specification[1]
a plurality of degenerate oligonucleotides for each codon to be mutagenized, wherein (i) the degenerate oligonucleotides each comprise a first homologous sequence and a plurality of degenerate triplet sequences;	When the difference between two homologues is one or more single point mutations in a codon, degenerate oligonucleotides can be used that encode the sequences in both homologues. One oligo may include many such degenerate codons... (Page 40, ll. 2-8) ...changes can be incorporated into homologue libraries using single degenerate codons at the corresponding positions...(Page 91, ll. 30-32) A protocol for single-stranded mutagenesis is described below...In the oligonucleotide, the region to be randomized can be represented by degenerate codons. (Col. 85, ll. 15-16, 23-24 of '679 patent)
(ii) the degeneracy of the triplet sequences includes multiple codons for all 20 amino acids; and	The codons at these positions can be NNN, NNK, or NNS which use 32 codons to encode all 20 residues. (Col. 86, ll. 13-15 of '679 patent)

New Claims 274-275	Support in the Specification[1]
(iii) each degenerate triplet sequences is N,N,N, N,N,G/C or N,N,G/T, wherein N is any nucleotide base or a derivative thereof; and	First, certain residues in a phage-displayed protein or peptide can be completely randomized. The codons at these positions can be NNN, NNK, or NNS which use 32 codons to encode all 20 residues. They can also be synthesized as preformed triplets or by mixing oligonucleotides synthesized by the split-resin method which together cover all 20 codons at each desired position. (Col. 86, ll. 12-18 of '679 patent) Table IV on pp. 99 equimolar amounts of each base for N, guanosine and cytosine for K, guanosine and thymidine for S (Col. 86, ll. 38-40 of '679 patent) novel base analogs such as inosine, 7-deaza dGTP (Dierick et al., Nucleic Acids Res. 21:4427-4428 (1993)) or other novel base analogs that improve the above properties. novel base analogs such as inosine, 7-deaza dGTP...7-deaza analogs...2' hydroxyl (Page 54, l. 37 - page 55, l. 14)
(b) subjecting the mutant polynucleotides to a screening and enrichment process that creates ligation-compatible ends near the ends of the mutant polynucleotides, so as to select one or more mutant polynucleotides encoding at least one desired property.	... a functional screen or selection is used to identify cells expressing functional protein. (Page 46, ll. 5-6) Page 30, l. 36 - page 31, line 26 ("fragments harboring the restriction enzyme recognition sites of interest, preferably near the ends of the fragment")

New Claims 274-275	Support in the Specification[1]
275. A method for producing a mutant polynucleotide encoding at least one desired property, the method comprising:	One aspect of the invention is a method for evolving a protein encoded by a DNA substrate molecule comprising... screening or selecting the products of (b) for a desired property... (Page 2, ll. 12-21)

New Claims 274-275	Support in the Specification[1]
(a) subjecting a plurality of parental polynucleotides to simultaneous mutagenesis so as to produce a plurality of mutant polynucleotides, wherein the mutagenesis comprises subjecting a codon-containing template polynucleotide to amplification	In some embodiments of the invention, sequence information from one or more substrate sequences is added to a given "parental" sequence of interest, with subsequent recombination between rounds of screening or selection. Typically, this is done with site-directed mutagenesis performed by techniques well known in the art... (Page 39, ll. 23-28) The "cassette" can be generated several different ways: A) by annealing two oligonucleotides together and converting them into double stranded DNA; B) by first amplifying segments of DNA with oligonucleotides that carry randomized sequences and then reamplifying the DNA to create the cassette for cloning; C) by first amplifying each half of the DNA segment with oligonucleotides that carry randomized sequences, and then heating the two pieces together to create the cassette for cloning; and D) by error-prone PCR. The cassettes formed by these four procedures are fixed in length and coding frame, but have codons which are unspecified at a low frequency. Thus, cloning and expression of the cassettes will generate a plurality of peptides or proteins that have one or more mutant residues along the entire length of the cassette. (Col. 85, l. 60 - Col. 86, l. 10 of U.S. Patent No. 6,117,679 ("the '679 patent"), which issued from Serial No. 08/621,859, incorporated by reference in its entirety for all purposes at p. 1, l. 12 of the specification)

New Claims 274-275	Support in the Specification[1]
using a degenerate oligonucleotide for each codon to be mutagenized, wherein the degenerate oligonucleotide comprises a first homologous sequence and a degenerate triplet sequence	When the difference between two homologues is one or more single point mutations in a codon, degenerate oligonucleotides can be used that encode the sequences in both homologues. One oligo may include many such degenerate codons... (Page 40, ll. 2-8) ...changes can be incorporated into homologue libraries using single degenerate codons at the corresponding positions...(Page 91, ll. 30-32) A protocol for single-stranded mutagenesis is described below...In the oligonucleotide, the region to be randomized can be represented by degenerate codons. (Col. 85, ll. 15-16, 23-24 of '679 patent)
wherein the degenerate triplet sequences is N,N,G/T, wherein N is any nucleotide base or a derivative thereof, and	First, certain residues in a phage-displayed protein or peptide can be completely randomized. The codons at these positions can be NNN, NNK, or NNS which use 32 codons to encode all 20 residues. They can also be synthesized as preformed triplets or by mixing oligonucleotides synthesized by the split-resin method which together cover all 20 codons at each desired position. (Col. 86, ll. 12-18 of '679 patent) Table IV on pp. 99 equimolar amounts of each base for N, guanosine and cytosine for K, guanosine and thymidine for S (Col. 86, ll. 38-40 of '679 patent)

New Claims 274-275	Support in the Specification[1]
(b) subjecting the mutant polynucleotides to a screening and enrichment process that creates ligation-compatible ends near the ends of the mutant polynucleotides, so as to select one or more mutant polynucleotides encoding at least one desired property.	... a functional screen or selection is used to identify cells expressing functional protein. (Page 46, ll. 5-6) Page 30, l. 36 - page 31, l. 26 ("fragments harboring the restriction enzyme recognition sites of interest, preferably near the ends of the fragment")